

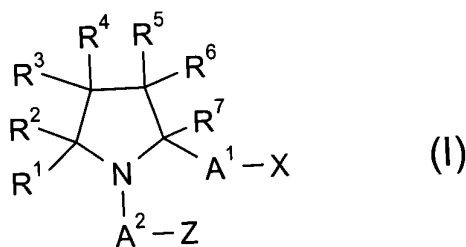
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Please amend the above-captioned application as follows:

In the Claims

Please cancel claims 57 and 58. Please amend claims 31, 32 and 59 without prejudice or disclaimer as follows (clean text; a marked-up copy of the amended claims is attached as an Appendix hereto):

~~31.~~ (Twice Amended) A compound of formula (I)



wherein

R¹ to R⁷ are independently selected from H, optionally substituted C₁₋₆ alkyl, C₂₋₆ alkenyl and C₂₋₆ alkynyl, optionally substituted aryl, OH, halogen, CN, OR¹², SR¹², COR¹², COOR¹², SOR¹², SO₂R¹², NR¹³R¹⁴, CONR¹³R¹⁴, SO₂NR¹³R¹⁴, where R¹³ and R¹⁴ are independently selected from H and C₁₋₃ alkyl and R¹² represents C₁₋₆ alkyl; two of R¹ to R⁷, together with the atoms connecting them, optionally form a 3- to 6-membered ring system; at least one of the pairs R¹ and R²; R³ and R⁴; and R⁵ and R⁶ is optionally replaced by an optionally substituted alkylidene group or =O; and two of R¹ to R⁷ which are positioned at adjacent carbon atoms are optionally replaced by a C-C bond;

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A¹ is selected from (-CR⁸R⁹-)_n, optionally substituted C₃₋₆ cycloalkylene and a combination of these groups, R⁸ and R⁹ being independently selected from H, C₁₋₆ alkyl, halogen, OH, OR¹² and NR¹³R¹⁴, where for n ≥ 2, R⁸ and R⁹ are the same or different in each group and two groups selected from R⁸ and R⁹ at adjacent C atoms are optionally replaced by a C-C bond, and a group -O- or -CO- is optionally positioned between two adjacent groups CR⁸R⁹; and wherein one of R⁸ and R⁹ is optionally combined with one of R¹ to R⁷ to form a 5- to 7-membered ring structure; and n = 1, 2, 3 or 4;

X is selected from COOM and groups which are capable of being converted into COOM under physiological conditions, M being selected from H and pharmaceutically acceptable cations;

A² is (-CR¹⁰R¹¹-)_m, where R¹⁰ and R¹¹ are independently selected from H, C₁₋₂ alkyl and halogen; where for m ≥ 2 the groups R¹⁰ and R¹¹ are the same or different in each group, a group -O- or -S- is optionally positioned between two adjacent groups -CR¹⁰R¹¹-, and two groups selected from R¹⁰ and R¹¹ at adjacent C atoms are optionally replaced by a C-C bond; and wherein one of R¹⁰ and R¹¹ is optionally combined with one of R¹ to R⁹ to form a 5- to 7-membered ring structure; and m is 1, 2, 3, or 4;

Z is selected from Y₃C-O-, Y₂C=CR¹⁵- and Y₂C=N-O-, where R¹⁵ is selected from H, C₁₋₃ alkyl or halogen and the groups Y are independently selected from optionally substituted C₆₋₁₂ aryl and optionally substituted C₂₋₅ heteroaryl having up to three heteroatoms

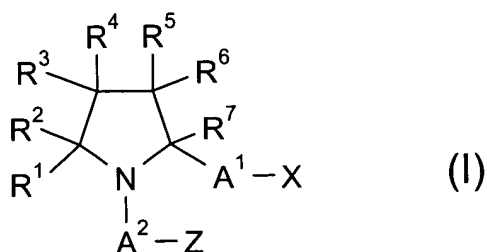
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independently selected from N, O and S, and the groups Y are optionally linked by a covalent bond or by groups between atoms belonging to different groups Y, said groups selected from -CH=CH-, -CH₂- and -CH₂CH₂-;

and the individual stereoisomers of these compounds.

2 ~~32.~~ (Amended) The compound of claim ~~31~~¹, wherein R⁷ is hydrogen and R¹ to R⁶ are independently selected from hydrogen, optionally substituted C₁₋₃ alkyl, halogen, OH, CN, and optionally substituted phenyl.

27 ~~59.~~ (Twice Amended) A pharmaceutical composition comprising at least one of a pharmaceutically acceptable carrier and a pharmaceutically acceptable excipient and at least one compound of formula (I):



wherein

R¹ to R⁷ are independently selected from H, optionally substituted C₁₋₆ alkyl, C₂₋₆

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alkenyl and C₂₋₆ alkynyl, optionally substituted aryl, OH, halogen, CN, OR¹², SR¹², COR¹², COOR¹², SOR¹², SO₂R¹², NR¹³R¹⁴, CONR¹³R¹⁴, SO₂NR¹³R¹⁴, where R¹³ and R¹⁴ are independently selected from H and C₁₋₃ alkyl and R¹² represents C₁₋₆ alkyl; two of R¹ to R⁷, together with the atoms connecting them, optionally form a 3- to 6-membered ring system; at least one of the pairs R¹ and R²; R³ and R⁴; and R⁵ and R⁶ is optionally replaced by an optionally substituted alkylidene group or =O; and two of R¹ to R⁷ which are positioned at adjacent carbon atoms are optionally replaced by a C-C bond;

A¹ is selected from (-CR⁸R⁹-)_n, optionally substituted C₃₋₆ cycloalkylene and a combination of these groups, R⁸ and R⁹ being independently selected from H, C₁₋₆ alkyl, halogen, OH, OR¹² and NR¹³R¹⁴, where for n ≥ 2, R⁸ and R⁹ are the same or different in each group and two groups selected from R⁸ and R⁹ at adjacent C atoms are optionally replaced by a C-C bond, and a group -O- or -CO- is optionally positioned between two adjacent groups CR⁸R⁹; and wherein one of R⁸ and R⁹ is optionally combined with one of R¹ to R⁷ to form a 5- to 7-membered ring structure; and n = 1, 2, 3 or 4;

X is selected from COOM and groups which are capable of being converted into COOM under physiological conditions, M being selected from H and pharmaceutically acceptable cations;

A² is (-CR¹⁰R¹¹-)_m, where R¹⁰ and R¹¹ are independently selected from H, C₁₋₂ alkyl and halogen; where for m ≥ 2 the groups R¹⁰ and R¹¹ are the same or different in each group, a

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group -O- or -S- is optionally positioned between two adjacent groups $-CR^{10}R^{11}-$, and two groups selected from R^{10} and R^{11} at adjacent C atoms are optionally replaced by a C-C bond; and wherein one of R^{10} and R^{11} is optionally combined with one of R^1 to R^9 to form a 5- to 7-membered ring structure; and m is 1, 2, 3, or 4;

Z is selected from Y_3C-O- , $Y_2C=CR^{15}-$ and $Y_2C=N-O-$, where R^{15} is selected from H, C_{1-3} alkyl or halogen and the groups Y are independently selected from optionally substituted C_{6-12} aryl and optionally substituted C_{2-5} heteroaryl having up to three heteroatoms independently selected from N, O and S, and the groups Y are optionally linked by a covalent bond or by groups between atoms belonging to different groups Y, said groups selected from $-CH=CH-$, $-CH_2-$ and $-CH_2CH_2-$.

REMARKS

The courtesy extended by Examiner Shameem to Applicants' representative during a personal interview on March 19, 2003 is acknowledged with appreciation. As discussed at the interview, reconsideration and withdrawal of the rejections made in the mentioned Office Action are respectfully requested, in view of the foregoing amendments and the following remarks.